

## **REMARKS**

In the Final Office Action mailed November 28, 2007, the Examiner rejected Claims 25, 26, 28-42, 45-55 and 65 under 35 U.S.C. §103(a) in light of Foldvari, et al., (2000) J. Controlled Release, Volume 66, 15 May 2000, pages 199-214 (hereinafter, "the Foldvari reference"), Baker et al., (1996) Nucleic Acids Research vol. 24, pages 2176-2182 (hereinafter, "the Baker reference"), U.S. Patent No. 6,267,987 (hereinafter, "the Park patent"), Banga, et al., Trends in Biotechnology 1998 vol 16(10) pages 408-412 (hereinafter, "the Banga reference"), and pages 1596 and 1597 of the 18<sup>th</sup> edition of Remington's Pharmaceutical Sciences, edited by Gennaro, 1990 (hereinafter, "the Remington reference"). Each rejection is addressed below.

### **I. Interview Conducted on February 20, 2008**

An interview was conducted on February 20, 2008 between Attorney of Record Robert Goetz and Examiner Fubara. The Interview involved a discussion pertaining to the Final Office Action, the references cited by the Examiner in the Final Office Action, and a proposed amendment to Claim 25.

### **II. Rejection of Claims 25, 26, 28-42, 45-55 and 65 under 35 U.S.C. §103(a)**

Claims 25, 26, 28-42, 45-55 and 65 were rejected under 35 U.S.C. §103(a) as being obvious in light of the Foldvari reference, Baker reference, the Park patent, the Banga reference, and the Remington reference. In particular, the Examiner stated, "Foldvari discloses transdermal delivery of protein or nucleotide to the skin tissue (pp. 71-86).<sup>1</sup> Foldvari discloses on page 205 that dendrimers are known to deliver DNA. Foldvari discloses cutaneous vaccination (title)...The combination of Foldvari and Baker discloses the use of dendrimers for the delivery of proteins or DNA...Skin patch membrane reads on transdermal delivery system and also on Foldvari's cutaneous vaccination (title)." Office Action, pages 3-7. The Applicants respectfully disagree.

None of the references cited by the Examiner, alone or in combination, teach a **skin-patch membrane** associated with at least one dendrimer comprising at least one biological agent comprising nucleic acid, and uses thereof, as recited in Claims 25 and 55. As such, none of the references cited by the Examiner teach all of the elements of the claimed invention.

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<sup>1</sup> The cited page reference does not pertain to the Foldvari reference.

However, in order to expedite prosecution without acquiescing with the Examiner's arguments, the Applicants now amend Claim 25 such that it recites, "...contacting said tissue with said composition such that said biological agent is transfected ~~said biological agent is provided~~ to said tissue at biologically active concentrations through said skin patch membrane." The Applicants reserve the right to prosecute previously presented Claim 1, or similar claims, at a future date. Support for this amendment is located throughout the Specification. For example, the Examiner is directed to Examples 9-13 which describe the successful transfection of nucleic acids within a biocompatible membrane to mice at biologically active concentrations.

The Foldvari reference does not teach the use of a **skin-patch membrane**. Moreover, the Foldvari reference does not teach the use of a **skin-patch membrane** associated with at least one dendrimer comprising at least one biological agent comprising nucleic acid, and the contacting of a tissue with the skin-patch membrane such that the biological agent is transfected to the tissue at biologically active concentrations through the skin patch membrane. On the contrary, the Foldvari reference only teaches specific forms of transdermal delivery devices including injection, gene gun delivery, jet injection, microfabricated microneedles, electroporation, sonophoration, and laser pulse delivery as its forms of cutaneous vaccination. See, Foldvari reference at pages 203-204 ("Delivery Devices"). Of note, the transdermal delivery devices described by the Foldvari reference do not include skin-patch membranes, as required in the claimed invention.

In order to overcome this deficiency, the Examiner relied upon the Banga reference and the Remington reference. In particular, the Examiner stated, "It is known in the prior art that transdermal delivery utilizes patch that is topically affixed to the skin as evidenced by [the Banga and Remington references]." Office Action, page 8. Respectfully, however, the Banga reference describes electroporation techniques for overcoming the limitations of *macromolecule* transdermal delivery techniques. See, e.g., page 408, first paragraph. As such, the Banga reference teaches away from the claimed invention (e.g., nucleic acid transfection to a skin tissue at biologically active concentrations through a skin patch membrane). Similarly, the Remington reference describes the transdermal delivery of drugs and medications – not nucleic acid transfection to a skin tissue at biologically active concentrations through a skin patch membrane.

The Examiner stated, "one skilled in the art, would be motivated by the teaching of the references taken together to use transdermal delivery devices comprising polyester or PAMAM

based dendrimers for delivery of nucleic acid/oligonucleotide/DNA via the skin of the subject by applying the transdermal device to the skin of the subject.” Office Action, page 6. Respectfully, the Applicants disagree. One skilled in the art would not be motivated to modify the transdermal delivery devices taught by Foldvari (e.g., injection, gene gun delivery, jet injection, microfabricated microneedles, electroporation, sonophoration, and laser pulse delivery) into a skin-patch delivery system as 1) none of the cited references teach the use of skin-patch delivery systems, as 2) the Foldvari reference provides no alternative delivery systems, and as 3) the Foldvari reference indicates the success of its described transdermal delivery devices. As noted above, neither the Banga nor the Remington references describe transdermal delivery of, for example, biological agents comprising nucleic acid. As such, one skilled in the art would have no motivation to combine the cited references in the manner suggested by the Examiner.

As such, none of the references cited by the Examiner, alone or in combination, teach all of the elements recited in Independent Claims 25 and 55. The Applicants request these rejections be withdrawn.

## **CONCLUSION**

Each rejection of the Final Office Action mailed November 28, 2007 has been addressed. Should the Examiner believe that a telephone interview would aid in the prosecution of this application Applicants encourage the Examiner to call the undersigned collect at (608) 218-6900.

Dated: March 24, 2008

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